

**REMARKS****Regarding the Status of the Claims:**

Claims 1-3, 6, 7, 12, 18, 22, 27, 29, 35, 42, 43, 48, 49, 56, 68, 74, 86, 90, 91, 121, 130, 132, 139, 145, 153, 156, 178, 179, 181, 186, and 193-214 are currently pending for reconsideration. Of these, claims 1, 90, 145, 153, 186, and 193 are in independent form.

Claims 1, 35, 43, 86, 90, 145, 153, and 193 are currently amended. The amendments to claims 1, 86, (which has been made dependent on claim 1), 90, and 145 are intended to better highlight novel features of the invention. The amendment to claim 6 is to correct dependency. The amendments to claims 43, 153 and 193 are made to improve the form thereof.

Claims 194-214 are new. Claims 194-199 are respectively dependent on claims 1, 86 and 90. Claims 200 and 205 are independent. New claims 201-204 and 214 are dependent on claim 200 and claims 206-213 are dependent on claim 205.

Claims 5, 13, 30, 74, 80, 81, 83, 105, 109, 111, and 155-156 are canceled hereby. Claims 4, 8-11, 14-17, 19-21, 23-26, 28, 31-34, 36-41, 44-47, 50-55, 57-67, 69-73, 75-79, 82, 84, 85, 87-89, 92-104, 106-108, 110, 112-120, 122-129, 131, 133-138, 140-144, 146-152, 154, 157-177, 180, 182-185, and 187-192 were previously canceled. Applicant reserves the right to prosecute all canceled claims in a continuing application.

**Regarding the Objections to the Claims:**

As to claim 22 applicants respectfully submit that the claim was entirely proper in its previous form in that the device is clearly state to be comprised of a gel which contains the indicated amount of water. As to claim 27, the term "active entity" is defined in the specification at page 24, lines 11-18. Moreover, claim 27 recites that the gel itself, which is a component of the device, and not something put into the device, comprises the active entity. As such, it is respectfully submitted that these claims are entirely proper, and that the objection should be withdrawn.

**Regarding the Rejection under 35 U.S.C. 112:**

The feature previously in canceled claim 13 has been added to claim 12.

As to claims 43 and 48, the Examiner is respectfully referred to the description in the specification at page 11, lines 14-26 and page 30, lines 5-15. It is respectfully

submitted that this clearly defines the meaning of both "interwell area" and "knife edged". Since the claims use the same terminology, it is respectfully submitte that these claims are not indefinite. If the Examiner persists in this rejection, he is respectfully requested to suggest alternative wording.

**Regarding the Rejections under 35 U.S.C. 102:**

**Bochner U.S. Patent 5,627,045 (Bochner):**

Claims 1-2, 42, 86, 145, 153, and 156 stand rejected as anticipated by Bochner. The Examiner's position is that the cited portions of the reference (Col. 8, line 35-Col. 9, line 9), and Figs. 1-4 disclose the embodiments of the invention recited in these claims. This rejection is respectfully traversed.

Independent claim 1 as amended, recites that:

the insides of said wells prevent loss or migration of cells during storage, movement, testing and observation, and inhibit or delay adhesion therein of living cells held in said wells.

Similarly, method claim 145 as amended recites:

forming the inside of said wells to prevent loss or migration of cells during storage, movement, testing and observation, and to inhibit or delay adhesion thereto of living cells held in said wells.

Independent claim 86 is directed to:

A carrier comprising a plurality of wells disposed on a surface each well configured to hold at least one living cell, the device characterized in that bottoms of said wells are flat.

Claim 153 is directed to a method of manipulating cells. As amended, this claim recites:

(a) providing a well-bearing component as described in claim 1 including a plurality of wells, wherein each well is configured to hold at least one living cell . . .

It is respectfully submitted that Bochner does not anticipate any of these claims, and in fact, teaches just the opposite as to some of the claimed features. Bochner is directed to a method of identifying microorganisms using standard well-bearing configurations with gel-forming matrices of various compositions. Neither in the

portions of the patent the cited by the Examiner, nor elsewhere, is there any disclosure, teaching, or suggestion that the wells are configured or formed to inhibit adhesion as in claims 1 and 145, or that the well bottoms are flat as in claim 86.

To the contrary, Bochner's wells are standard, and the gel inside the wells adheres the cells to the wells. The Examiner argues that the cells in Bochner do not adhere to the wells, but this is not correct. The cells adhere to the wells in the same way that pieces of fruit in a bowl of Jello adhere to the bowl.

Likewise, since Bochner fails to disclose, teach, or suggest the device of claim 1, it can also not anticipate claim 153.

Nor does Bochner disclose, teach, or suggest a gel carrier as in claim 80.

Claims 2, and 42 are dependent on claim 1. These claims are not anticipated by Bochner for the same reasons as their parent claims and further because they recite features, which, when considered in combination with their parent claims, are also not anticipated by Bochner.

Kim et al. U.S. patent publication 2003/0030184 (Kim):

Claims 1-3, 7, 35, 42-43, 49, 68, 74, 121, 130, 132, 139, 145, and 193 stand rejected as anticipated by Kim. The Examiner's position is that the cited paragraphs (135, 138, 142-143, 190-199, 206, 208, and 215) and Figs. 1a, 1b, and 2a, disclose the embodiments of the invention recited in these claims. This rejection is respectfully traversed.

Preliminarily, it is noted that claim 185 (which was previously canceled) is mentioned in the general statement of this rejection in the second full paragraph on page 4 of the Office Action, but are not mentioned subsequently. Further, claims 86 and 186 are not mentioned in the general statement of the rejection, but claim 86 is discussed in the third paragraph on page 4 and on page 6. The discussion on page 6, however, appears to be referring to the recitations of claim 83. Also, claim 186 is discussed in detail in the first paragraph on page 7. It is therefore assumed that the Examiner intended to include claims 83, 86, and 186 in the rejection under Kim, but not claim 185. The rejection of claim 83 is moot as this claim has currently been canceled.

In any event, Kim fails to disclose, teach, or suggest any structure reasonably corresponding to wells having the claimed features. In particular, Kim does not disclose, teach, or suggest wells (or any other structure) that confine cells therein against loss or migration during storage, movement, testing and observation, and/or

inhibits or delays adhesion or proliferation as in claims 1, 86, and 145. To the contrary, Kim discloses a multilayer structure formed by a base plate and an overlying stencil with openings to immobilize cells *before*, and only before, testing and observation. The cells rest on the base, and the openings in the stencil define the areas on which the cells rest. Kim's device is expressly designed so that the stencil is removable specifically for the purpose of allowing the cells to escape to permit study of cell motility.

In addition, the base plate is coated with a substance that at least temporarily immobilizes the cells in these areas, the opposite of what is recited in claims 1, 145, 153, 200 and 206.

Further, Kim does not disclose, teach, or suggest a well which is expandable as in claim 186.

Likewise, since Kim fails to disclose, teach, or suggest the device of claim 1, it can also not anticipate claim 121.

Kim supports applicant's interpretation throughout the disclosure. Below are some representative examples:

In paragraph [0017], Kim refers **to** study of cell motility, either in response to a cell affecting agent, or random motility, and says it is desirable to be able to monitor cellular movement from a predefined position. This is done by immobilizign cells upon cells simply to attach themselves to a suitable surface, such as glass or plastic, and then allowing them to migrate into adjacent areas.

In contrast, the rejected claims recite wells that confine cells *during testing and observation*, but which inhibit or delay adherence to the wells. Kim immobilizes only *before* performing migration testing.

In paragraph [0023], Kim describes "micro-regions" on a support layer, "micro-orifices" on a first (stencil) layer, and "macro-orifices" on a second (stencil) layer. There is no reference to immobilization in wells. In fact, the description mentions "wells" for example, only in paragraph [0142] concerning orifice size, or in paragraphs [0198], [0199], and [0281] where the discussion focuses on attachment to the base layer or patterning in micro-regions *before* stencil removal for motility testing.

In paragraphs [0055], [0058], and [135], the support, i.e., base layer, is described as having at least one cell of a plurality of cells in each respective micro-region *on the support...* the cells thereby being arrayed on the support in a pattern that corresponds to the pattern of the micro-orifices... Removing said first and second layer **allows** monitoring cells for movement or lack of movement **away from the micro-regions**.

Immobilization is described as on *the support*, not in wells. When first and second stencil layers are removed, the cells are no longer confined, which is essential for motility testing. Thus, the cells to migrate, contrary to what is recited in the rejected claims.

Numerous other references in Kim emphasize the basic difference compared to what is described in the rejected claims.

Claims 2, 5, 6, 7, 35, 42, 49, 68, 74, and 86 are dependent on claim 1, and claims 130, 132, and 139 are dependent on claim 121. These claims are not anticipated by Kim for the same reasons as their parent claims and further because they recite features, which, when considered in combination with their parent claims, are also not disclosed, taught or suggested by Kim.

Claim 186 recites, among its other features, "c) increasing the size of said well so as to provide an increased space for proliferation of said cell." There is no mention of this in paragraph [208] of Kim cited by the Examiner, or anywhere else in Kim. Claim 186 is accordingly not anticipated by Kim.

Finally, claim 193 is directed to A method of collecting cells from a biological sample. This claim as amended recites:

- (a) providing a well-bearing device, said well-bearing device having:

- (i) a plurality of wells disposed on a surface, each well configured to hold at least one cell;
  - and (ii) a plurality of protuberances protruding from said surface; and

- (b) contacting the biological sample with said surface so as to remove cells from the biological sample.

This claim is also not anticipated by Kim. There is no disclosure, teaching, or suggestion in paragraphs 135 and 208 of a surface having protuberances, or of removing cells from a biological sample by contacting the sample with said surface.

**Regarding the Rejections under 35 U.S.C. 103:**

Claims 12 and 90 are rejected as "being anticipated by" Kim in light of Sanghera et al. U.S. patent 5,525,800 (Sanghera) and Hahn et al. U.S. patent publication

2003/0017079 (Hahn). While these claims have been rejected as "anticipated", it is understood as being under 35 U.S.C. 103 because multiple references have been applied. As so understood, applicants traverse the rejection of claim 12 because it is dependent on claim 1, and is therefore patentable over Kim for the reasons stated above. Neither Sanghera nor Hahn overcomes the deficiencies in Kim. Hahn is directed to gel compositions, while Sanghera deals with a fiber optic detector. Neither reference discloses, teaches, or suggests wells that confine cells in wells against loss or migration.

Claim 90 has been amended to recite that the device is characterized in that said wells confine cells therein. This claim is therefore also not rendered unpatentable over Kim in view of Sanghera and Hahn, as stated above.

Claim 91 has also been rejected as unpatentable over Kim in view of Sanghera and Hahn. However, this claim is dependent on claim 90, and is also allowable over Kim in view of Sanghera and Hahn for the reasons stated above.

Claims 18, 22, 27, and 29 stand rejected as unpatentable over Kim in view of Ravkin U.S. patent publication 2003/0030184 (Ravkin). This rejection is respectfully traversed.

Ravkin does not overcome the deficiencies in Kim discussed above. The Examiner has cited Ravkin for its teaching of what he interprets the "outer layer" mentioned in paragraph [0090] as a gel cover. The Examiner's interpretation is overly expansive. Ravkin does not suggest a cover. His outer layer is just part of the well structure.

Claims 18, 22, 27, and 29 are all dependent on claim 1. These claims are patentable for all the same reasons as claim 1, and for the additional reason stated immediately above.

Claims 178, 179, and 181 stand rejected as unpatentable over Bochner in view of Kim. This rejection is also traversed. Claim 153, on which these claims depend, is not anticipated by Bochner because Bochner fails to disclose, teach, or suggest the features of claim 1 as amended, which are incorporated in claim 153, as discussed above. Kim likewise fails to disclose, teach, or suggest these features, also as discussed above. Thus, irrespective of what else is found in Kim, it fails to rectify the basic deficiency in Bochner relative to claim 1. Claims 178, 179, and 181 are accordingly not rendered unpatentable over Bochner in view of Kim.

New Claims 194-214:

New claims 194-199 are dependent on claims 193, 1, 80, 86 and 90, the patentability of which has been discussed in detail above. Claims 194-199 are patentable for the same reasons.

New Claim 200 recites:

A device for holding living cells, ...

characterized in that the insides of said wells delay or inhibit adhesion or proliferation of cells to the insides of said wells.

As discussed above, both Bochner and Kim are constructed in exactly the opposite way, i.e., to *promote* adhesion and/or proliferation. Claim 200 is accordingly allowable.

Claims 201-204 and 214 are dependent on claim 200 and are allowable for the same reasons.

New claim 205 recites:

A method of making a cell-study device comprising...

forming the insides of the wells to delay or inhibit adhesion to walls of said wells, or to delay or inhibit proliferation of living cells held in the wells.

The arguments above with respect to claim 200 is applicable here as well. Claim 205 should therefore be allowed for the same reason.

Claims 206-213 are dependent on claim 205 and are also allowable for the same reason.

In view of the foregoing amendments and arguments, it is respectfully submitted that the application is in condition for allowance, and early notice thereof is respectfully solicited.

Respectfully submitted,

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